

## **REMARKS**

Applicants maintain that the examination should be extended to all methods defined in claim 1. A search and examination directed to the subject matter of claim 1 has not been shown to be unduly burdensome. Such a search and examination would be prescribed by the use of particular compounds, i.e., ureas, having heteroaryl groups further substituted by aryl or heteroaryl groups. This search and examination would be further prescribed by the diseases to be treated, which are mediated by p38. While the compounds may be classified in separate subclasses, the methods for their use in treating p38 mediated diseases have not been shown to be separately classified.

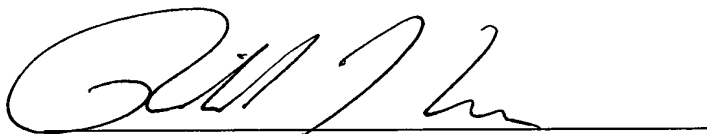
### **Rejection Under 35 USC §103**

Applicants submit the language within Regan et al. (U.S. 6,080,763) has not been shown to be prior art to their invention. Applicants' disclosure and claims antedate the filing date of U.S. 6,080,763. Regan et al. claims priority to provisional application 60/064,102 but no evidence has been presented that this provisional application contains the disclosure relied on in rejecting the claims.

### **New claims 17-30**

New claims 17-30 are directed to embodiments wherein the ureas employed have a bridged cyclic structure for "B". Compounds with this structure are not shown or suggested by Regan.

Respectfully submitted,



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**Filed: March 15, 2002**

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**VERSION WITH MARKINGS TO SHOW CHANGES MADE**

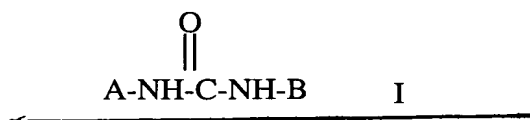
**IN THE CLAIMS**

**Claims 1, 4, 12 and 13 have been amended as follows:**

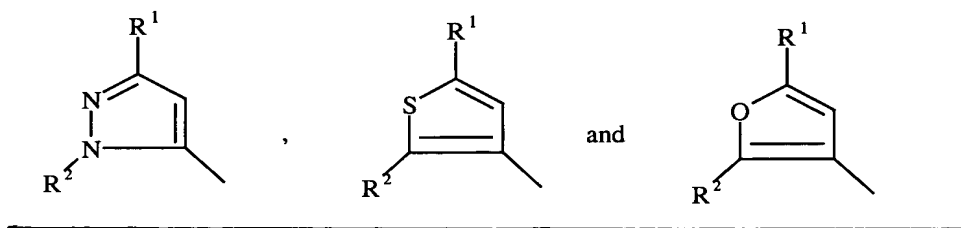
**1. (Amended)** A method for the treatment of a disease other than cancer mediated by



p38 which comprises administering a compound of formula I or a pharmaceutically acceptable salt thereof

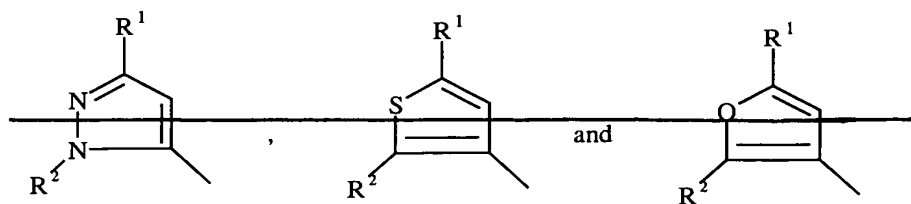


wherein A is a heteroaryl selected from the group consisting of



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wherein  $\text{R}^1$  is selected from the group consisting of  $\text{C}_3\text{-C}_{10}$  alkyl,  $\text{C}_3\text{-C}_{10}$  cycloalkyl, up to per-halosubstituted  $\text{C}_1\text{-C}_{10}$  alkyl and up to per-halosubstituted  $\text{C}_3\text{-C}_{10}$



cycloalkyl;

B is a substituted or unsubstituted, up to tricyclic, aryl or heteroaryl moiety of up to 30 carbon atoms with at least one 5- or 6-member aromatic structure containing 0-4 members of the group consisting of nitrogen, oxygen and sulfur, wherein if B is a substituted group, it is substituted by one or more substituents independently selected from the group consisting of halogen, up to per-halosubstitution, and  $X_n$ ,

wherein n is 0-3 and each X is independently selected from the group consisting of  $-CN$ ,  $-CO_2R^5$ ,  $-C(O)NR^5R^{5'}$ ,  $-C(O)R^5$ ,  $-NO_2$ ,  $-OR^5$ ,  $-SR^5$ ,  $-NR^5R^{5'}$ ,  $-NR^5C(O)OR^{5'}$ ,  $-NR^5C(O)R^{5'}$ ,  $C_1$ - $C_{10}$  alkyl,  $C_2$ - $C_{10}$ -alkenyl,  $C_1$ - $C_{10}$ -alkoxy,  $C_3$ - $C_{10}$  cycloalkyl,  $C_6$ - $C_{14}$  aryl,  $C_7$ - $C_{24}$  alkaryl,  $C_3$ - $C_{13}$  heteroaryl,  $C_4$ - $C_{23}$  alkheteroaryl, substituted  $C_1$ - $C_{10}$  alkyl, substituted  $C_2$ - $C_{10}$ -alkenyl, substituted  $C_1$ - $C_{10}$ -alkoxy, substituted  $C_3$ - $C_{10}$  cycloalkyl, substituted  $C_4$ - $C_{23}$  alkheteroaryl and  $-Y-Ar$ ;

where X is a substituted group, it is substituted by one or more substituents independently selected from the group consisting of  $-CN$ ,  $-CO_2R^5$ ,  $-C(O)R^5$ ,  $-C(O)NR^5R^{5'}$ ,  $-OR^5$ ,  $-SR^5$ ,  $-NR^5R^{5'}$ ,  $-NO_2$ ,  $-NR^5C(O)R^{5'}$ ,  $-NR^5C(O)OR^{5'}$  and halogen up to per-halosubstitution;

wherein  $R^5$  and  $R^{5'}$  are independently selected from H,  $C_1$ - $C_{10}$  alkyl,  $C_2$ - $C_{10}$ -alkenyl,  $C_3$ - $C_{10}$  cycloalkyl,  $C_6$ - $C_{14}$  aryl,  $C_3$ - $C_{13}$  heteroaryl,  $C_7$ - $C_{24}$  alkaryl,  $C_4$ - $C_{23}$  alkheteroaryl, up to per-halosubstituted  $C_1$ - $C_{10}$  alkyl, up to per-halosubstituted  $C_2$ - $C_{10}$ -alkenyl, up to per-halosubstituted  $C_3$ - $C_{10}$  cycloalkyl, up to per-halosubstituted  $C_6$ - $C_{14}$  aryl and up to per-halosubstituted  $C_3$ - $C_{13}$  heteroaryl,

wherein Y is  $-O-$ ,  $-S-$ ,  $-N(R^5)-$ ,  $-(CH_2)_m-$ ,  $-C(O)-$ ,  $-CH(OH)-$ ,  $-(CH_2)_mO-$ ,  $-NR^5C(O)NR^5R^{5'}$ ,  $-NR^5C(O)-$ ,  $-C(O)NR^5-$ ,  $-(CH_2)_mS-$ ,  $-(CH_2)_mN(R^5)-$ ,  $-O(CH_2)_m-$ ,  $-CHX^a-$ ,  $-CX^a_2-$ ,  $-S-(CH_2)_m-$  and  $-N(R^5)(CH_2)_m-$ ,

$m = 1-3$ , and  $X^a$  is halogen; and

Ar is a 5-10 member aromatic structure containing 0-2 members of the group consisting of nitrogen, oxygen and sulfur which is unsubstituted or substituted by halogen up

to per-halosubstitution and optionally substituted by  $Z_{n1}$ , wherein  $n1$  is 0 to 3 and each  $Z$  is independently selected from the group consisting of  $-\text{CN}$ ,  $-\text{CO}_2\text{R}^5$ ,  $-\text{C}(\text{O})\text{NR}^5\text{R}^{5'}$ ,  $-\text{C}(\text{O})\text{NR}^5$ ,  $-\text{NO}_2$ ,  $-\text{OR}^5$ ,  $-\text{SR}^5$ ,  $-\text{NR}^5\text{R}^{5'}$ ,  $-\text{NR}^5\text{C}(\text{O})\text{OR}^{5'}$ ,  $-\text{OC}(\text{O})\text{R}^5$ ,  $-\text{NR}^5\text{C}(\text{O})\text{R}^{5'}$ ,  $\text{C}_1\text{-C}_{10}$  alkyl,  $\text{C}_3\text{-C}_{10}$  cycloalkyl,  $\text{C}_6\text{-C}_{14}$  aryl,  $\text{C}_3\text{-C}_{13}$  heteroaryl,  $\text{C}_7\text{-C}_{24}$  alkaryl,  $\text{C}_4\text{-C}_{23}$  alkheteroaryl, substituted  $\text{C}_1\text{-C}_{10}$  alkyl, substituted  $\text{C}_3\text{-C}_{10}$  cycloalkyl, substituted  $\text{C}_7\text{-C}_{24}$  alkaryl and substituted  $\text{C}_4\text{-C}_{23}$  alkheteroaryl;

wherein if  $Z$  is a substituted group, it is substituted by the one or more substituents independently selected from the group consisting of  $-\text{CN}$ ,  $-\text{CO}_2\text{R}^5$ ,

$-\text{C}(\text{O})\text{NR}^5\text{R}^{5'}$ ,  $-\text{OR}^5$ ,  $-\text{SR}^5$ ,  $-\text{NO}_2$ ,  $-\text{NR}^5\text{R}^{5'}$ ,  $-\text{NR}^5\text{C}(\text{O})\text{R}^{5'}$  and  $-\text{NR}^5\text{C}(\text{O})\text{OR}^{5'}$ , and

wherein  $\text{R}^2$  is  $\text{C}_6\text{-C}_{14}$  aryl,  $\text{C}_3\text{-C}_{14}$  heteroaryl, substituted  $\text{C}_6\text{-C}_{14}$  aryl or substituted  $\text{C}_3\text{-C}_{14}$  heteroaryl,

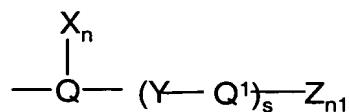
wherein if  $\text{R}^2$  is a substituted group, it is substituted by one or more substituents independently selected from the group consisting of halogen, up to per-halosubstitution, and  $\text{V}_n$ ,

wherein  $n = 0\text{-}3$  and each  $\text{V}$  is independently selected from the group consisting of  $-\text{CN}$ ,  $-\text{CO}_2\text{R}^5$ ,  $-\text{C}(\text{O})\text{NR}^5\text{R}^{5'}$ ,  $-\text{OR}^5$ ,  $-\text{SR}^5$ ,  $-\text{NR}^5\text{R}^{5'}$ ,  $-\text{C}(\text{O})\text{R}^5$ ,  $-\text{OC}(\text{O})\text{NR}^5\text{R}^{5'}$ ,  $-\text{NR}^5\text{C}(\text{O})\text{OR}^{5'}$ ,  $-\text{SO}_2\text{R}^5$ ,  $-\text{SOR}^5$ ,  $-\text{NR}^5\text{C}(\text{O})\text{R}^{5'}$ ,  $-\text{NO}_2$ ,  $\text{C}_1\text{-C}_{10}$  alkyl,  $\text{C}_3\text{-C}_{10}$  cycloalkyl,  $\text{C}_6\text{-C}_{14}$  aryl,  $\text{C}_3\text{-C}_{13}$  heteroaryl,  $\text{C}_7\text{-C}_{24}$  alkaryl,  $\text{C}_4\text{-C}_{24}$  alkheteroaryl, substituted  $\text{C}_1\text{-C}_{10}$  alkyl, substituted  $\text{C}_3\text{-C}_{10}$  cycloalkyl, substituted  $\text{C}_6\text{-C}_{14}$  aryl, substituted  $\text{C}_3\text{-C}_{13}$  heteroaryl, substituted  $\text{C}_7\text{-C}_{24}$  alkaryl and substituted  $\text{C}_4\text{-C}_{24}$  alkheteroaryl,

where  $\text{V}$  is a substituted group, it is substituted by one or more substituents independently selected from the group consisting of halogen, up to per-halosubstitution,  $-\text{CN}$ ,  $-\text{CO}_2\text{R}^5$ ,  $-\text{C}(\text{O})\text{R}^5$ ,  $-\text{C}(\text{O})\text{NR}^5\text{R}^{5'}$ ,  $-\text{NR}^5\text{R}^{5'}$ ,  $-\text{OR}^5$ ,  $-\text{SR}^5$ ,  $-\text{NR}^5\text{C}(\text{O})\text{R}^{5'}$ ,  $-\text{NR}^5\text{C}(\text{O})\text{OR}^{5'}$  and  $-\text{NO}_2$ ,

wherein  $\text{R}^5$  and  $\text{R}^{5'}$  are each independently as defined above.

4. A method of claim 1, wherein B is



wherein

Y is selected from the group consisting of -O-, -S-, -CH<sub>2</sub>-, -SCH<sub>2</sub>-, -CH<sub>2</sub>S-,  
-CH(OH)-, -C(O)-, -CX<sup>a</sup><sub>2</sub>, -CX<sup>a</sup>H-, -CH<sub>2</sub>O- and -OCH<sub>2</sub>-,

X<sup>a</sup> is halogen,

Q is a six member aromatic structure containing 0-2 nitrogen, substituted or unsubstituted by halogen, up to per-halosubstitution;

Q<sup>1</sup> is a mono- or bicyclic aromatic structure of 3 to 10 carbon atoms and 0-4 members of the group consisting of N, O and S, ~~unsubstituted~~ substituted or unsubstituted by halogen up to per-halosubstitution,

s = 0 or 1, and

X, Z, n and n1 are as defined in claim 1.

**12.** A method according to claim 1, wherein R<sup>2</sup> R<sup>1</sup> is t-butyl.

**13.** A method according to claim + 12, comprising administering an amount of a compound of formula I effective to inhibit p38.

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